



cleidocranial dysplasia

Cleidocranial dysplasia is a condition that primarily affects the development of the bones and teeth. Signs and symptoms of cleidocranial dysplasia can vary widely in severity, even within the same family.

Individuals with cleidocranial dysplasia usually have underdeveloped or absent collarbones (clavicles). As a result, their shoulders are narrow and sloping, can be brought unusually close together in front of the body, and in some cases the shoulders can be made to meet in the middle of the body. Delayed closing of the spaces between the bones of the skull (fontanelles) is also characteristic of this condition. The fontanelles usually close in early childhood, but may remain open into adulthood in people with this disorder.

Affected individuals may be 3 to 6 inches shorter than other members of their family, and may have short, tapered fingers and broad thumbs; short forearms; flat feet; knock knees; and an abnormal curvature of the spine (scoliosis). Characteristic facial features may include a wide, short skull (brachycephaly); a prominent forehead; wide-set eyes (hypertelorism); a flat nose; and a small upper jaw.

Individuals with cleidocranial dysplasia may have decreased bone density (osteopenia) and may develop osteoporosis, a condition that makes bones progressively more brittle and prone to fracture, at a relatively early age. Women with cleidocranial dysplasia have an increased risk of requiring a cesarean section when delivering a baby, due to a narrow pelvis preventing passage of the infant's head.

Dental abnormalities seen in cleidocranial dysplasia may include delayed loss of the primary (baby) teeth; delayed appearance of the secondary (adult) teeth; unusually shaped, peg-like teeth; misalignment of the teeth and jaws (malocclusion); and extra teeth, sometimes accompanied by cysts in the gums.

In addition to skeletal and dental abnormalities, people with cleidocranial dysplasia may have hearing loss and be prone to sinus and ear infections. Some young children with this condition are mildly delayed in the development of motor skills such as crawling and walking, but intelligence is unaffected.

Frequency

Cleidocranial dysplasia occurs in approximately 1 per million individuals worldwide.

Genetic Changes

The *RUNX2* gene provides instructions for making a protein that is involved in bone and cartilage development and maintenance. This protein is a transcription factor,

which means it attaches (binds) to specific regions of DNA and helps control the activity of particular genes. Researchers believe that the RUNX2 protein acts as a "master switch," regulating a number of other genes involved in the development of cells that build bones (osteoblasts).

Some mutations change one protein building block (amino acid) in the RUNX2 protein. Other mutations introduce a premature stop signal that results in an abnormally short protein. Occasionally, the entire gene is missing.

These genetic changes reduce or eliminate the activity of the protein produced from one copy of the *RUNX2* gene in each cell, decreasing the total amount of functional RUNX2 protein. This shortage of functional RUNX2 protein interferes with normal bone and cartilage development, resulting in the signs and symptoms of cleidocranial dysplasia. In rare cases, affected individuals may experience additional, unusual symptoms resulting from the loss of other genes near *RUNX2*.

In about one-third of individuals with cleidocranial dysplasia, no mutation in the *RUNX2* gene has been found. The cause of the condition in these individuals is unknown.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, an affected person inherits the mutation from one affected parent. Other cases may result from new mutations in the gene. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- cleidocranial dysostosis
- Marie-Sainton syndrome

Diagnosis & Management

These resources address the diagnosis or management of cleidocranial dysplasia:

- GeneReview: Cleidocranial Dysplasia
<https://www.ncbi.nlm.nih.gov/books/NBK1513>
- Genetic Testing Registry: Cleidocranial dysostosis
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0008928/>
- MedlinePlus Encyclopedia: Cleidocranial dysostosis
<https://medlineplus.gov/ency/article/001589.htm>

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Cleidocranial dysostosis
<https://medlineplus.gov/ency/article/001589.htm>
- Health Topic: Craniofacial Abnormalities
<https://medlineplus.gov/craniofacialabnormalities.html>

Genetic and Rare Diseases Information Center

- Cleidocranial dysplasia
<https://rarediseases.info.nih.gov/diseases/6118/cleidocranial-dysplasia>

Educational Resources

- Disease InfoSearch: Cleidocranial Dysplasia
<http://www.diseaseinfosearch.org/Cleidocranial+Dysplasia/1683>
- MalaCards: cleidocranial dysplasia
http://www.malacards.org/card/cleidocranial_dysplasia

Patient Support and Advocacy Resources

- AmeriFace
<http://www.ameriface.org/>
- Children's Craniofacial Association
<http://www.ccakids.com/>
- National Organization for Rare Disorders (NORD)
<http://rarediseases.org/rare-diseases/cleidocranial-dysplasia/>

GeneReviews

- Cleidocranial Dysplasia
<https://www.ncbi.nlm.nih.gov/books/NBK1513>

Genetic Testing Registry

- Cleidocranial dysostosis
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0008928/>

Scientific articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Cleidocranial+Dysplasia%5BMAJR%5D%29+AND+%28cleidocranial+dysplasia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- CLEIDOCRANIAL DYSPLASIA
<http://omim.org/entry/119600>

Sources for This Summary

- OMIM: CLEIDOCRANIAL DYSPLASIA
<http://omim.org/entry/119600>
- Cohen MM Jr. The new bone biology: pathologic, molecular, and clinical correlates. *Am J Med Genet A*. 2006 Dec 1;140(23):2646-706. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17103447>
- GeneReview: Cleidocranial Dysplasia
<https://www.ncbi.nlm.nih.gov/books/NBK1513>
- Hermanns P, Lee B. Transcriptional dysregulation in skeletal malformation syndromes. *Am J Med Genet*. 2001 Winter;106(4):258-71. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11891677>
- Lo Muzio L, Tetè S, Mastrangelo F, Cazzolla AP, Lacaïta MG, Margaglione M, Campisi G. A novel mutation of gene CBFA1/RUNX2 in cleidocranial dysplasia. *Ann Clin Lab Sci*. 2007 Spring;37(2):115-20.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17522365>
- Otto F, Kanegane H, Mundlos S. Mutations in the RUNX2 gene in patients with cleidocranial dysplasia. *Hum Mutat*. 2002 Mar;19(3):209-16. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11857736>
- Pal T, Napierala D, Becker TA, Loscalzo M, Baldrige D, Lee B, Sutphen R. The presence of germ line mosaicism in cleidocranial dysplasia. *Clin Genet*. 2007 Jun;71(6):589-91.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17539909>
- Rice DP. Craniofacial anomalies: from development to molecular pathogenesis. *Curr Mol Med*. 2005 Nov;5(7):699-722. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16305494>

- Schroeder TM, Jensen ED, Westendorf JJ. Runx2: a master organizer of gene transcription in developing and maturing osteoblasts. Birth Defects Res C Embryo Today. 2005 Sep;75(3):213-25. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16187316>
 - Segal N, Puterman M. Cleidocranial dysplasia - review with an emphasis on otological and audiological manifestations. Int J Pediatr Otorhinolaryngol. 2007 Apr;71(4):523-6. Epub 2007 Jan 18. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17239447>
-

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/cleidocranial-dysplasia>

Reviewed: January 2008

Published: January 3, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services